



Risk Associated with Obesity and Its Related Lifestyle Factors: What About Cancer?

Cheryl L. Albright PhD, MPH
Associate Professor

Social and Behavioral Sciences Program
Cancer Research Center of Hawaii
University of Hawaii at Manoa

The leading causes of death in the United States are cardiovascular diseases and cancer.¹ It has been estimated that 14% of total mortality or over 300,000 deaths a year could be prevented through lifestyle changes such as diet and exercise.² Another analysis attributed 325,000 deaths a year in non-smokers to obesity.³ Hawaii has a unique, ethnically diverse population consisting of Asians, Hawaiians, Pacific Islanders, African Americans, and Whites.⁴ However, the leading causes of death are no different here than in the rest of the nation.⁵ But, there are considerable differences across Hawaii's ethnic groups for specific causes of death and for disease specific incidence rates, especially site-specific cancers like breast cancer.⁶ For example, in Hawaii, breast cancer is the leading cancer diagnosis for women regardless of race, with Hawaiian women having the highest incidence of breast cancer and the highest rates of breast cancer mortality.^{7,8} Lifestyles issues such as nutrition, physical inactivity, and obesity contribute to these ethnic differences in cancer incidence and mortality.^{6,9} This article will review recent research linking obesity with cancer, especially breast cancer, and the lifestyle factors that impact adults' weight.

Table 1.— Two Formulas for Calculating Body Mass Index (BMI)

$$\text{BMI} = \frac{\text{Weight in Pounds}}{(\text{Height in inches})^2} \times 703$$

or

$$\frac{\text{Weight in Kilograms}}{(\text{Height in meters})^2}$$

Categories of BMI:

	BMI
Underweight	< 18.5
Normal	18.5-24.9
Overweight	25-29.9
Obese	> 30
Obese I	30.0 – 34.9
Obese II	35-39.9
Obese III	>40

For a 5' 5" person weighing:

100 lbs.,	BMI = 17 (underweight)
138 lbs.,	BMI = 23 (normal)
162 lbs.,	BMI = 27 (overweight)
186 lbs.,	BMI = 31 (Level I obese)
247 lbs.,	BMI = 41 (Level III obese)

Defining Obesity and Overweight

Although several measures of obesity exist, the one used in epidemiological research is also the one most easily assessed in clinical practices, it is known as Body Mass Index or BMI. BMI is a measure that takes into consideration the patient's weight relative to their height. Once the BMI is calculated, the BMI score or BMI level can be used to define risk categories, for example: underweight, normal weight, overweight, and obese [10]. The formulas for calculating BMI, and examples of the BMI level corresponding to four different weights for a given height (5' 5") are listed in Table 1.

There is a website that calculates the BMI for a specific height and weight: (<http://www.nhlbi.support.com/bmi/>), and a website that provides a table with the BMI level for hundreds of height/weight combinations (http://www.nhlbi.nih.gov/guidelines/obesity/bmi_tbl.htm). Although BMI is highly correlated with percent body fat, it can misclassify the fat levels of individuals with large amounts of muscle mass (e.g., athletes or body-builders). However, for the vast majority of people BMI represents an excess in body fat, and this excess fat brings an increased risk for chronic diseases, including cancer. The distribution of fat throughout the body can also connote risk. The National Heart, Lung and Blood Institute recommends that waist circumference also be used as an indicator of

abdominal fat (http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/profmats.htm). In the interest of brevity, this article will focus on BMI as a weight-related indicator of risk.

Prevalence of Obesity in United States and in Hawaii

There is a growing epidemic of obesity in the U.S. and Hawaii, and the epidemic is spreading fast. In 2001, 58% of U.S. adults had a BMI \geq 25, indicating they were overweight, and 18% were obese (BMI \geq 30).¹¹ This represents over 180 million people, and this percentage has risen, annually over the last two decades. A graphic depiction of the progression of this epidemic over 16 years can be found on the Centers for Disease Control and Prevention (CDCP) website (<http://www.cdc.gov/nccdphp/dnpa/obesity/trend/maps/index.htm>). The CDCP website has a series of maps of the United States, with colors showing the prevalence of obesity in each state from 1985 to 2001. It has been estimated that the economic costs of this epidemic of obesity approaches \$117 billion per year.

In Hawaii, the prevalence of overweight is 51% for adults, with 18% being obese in 2001.¹¹ Although these levels are slightly lower than the nation-wide rates, there are significant differences in the

prevalence of obesity across ethnic groups in Hawaii.^{11,12} The prevalence of overweight (BMI ≥ 25) in adults from a specific ethnic group is 71% for Hawaiian/Part Hawaiian, 48% for Whites, 47% for Japanese, and 44% for Filipino.¹² Also, between and within ethnic groups the prevalence of obesity can vary depending on gender, age, level of education, and income.

Some of the differences in obesity across ethnicities may have a genetic basis. For example, in a study of 560 adults, the percentage of indigenous ancestry among native Hawaiians was found to be significantly associated with BMI, after adjusting for age, physical activity, and total energy intake.¹³ Estimates of the heritability for obesity range from less than 20% to almost 90%.¹⁴⁻¹⁷ Nevertheless, lifestyle factors, specifically diet and exercise practices, can contribute significantly to weight gain/obesity due to an imbalance between calories "in" and calories "out". Although it can be difficult for some patients to control their weight, obesity is considered a modifiable risk factor. Research also indicates that personal characteristics such as obesity and the psychosocial sequelae that occur, such as poor body image and low self-esteem may also result in lower usage of cancer screening services such as mammography.^{18,19} Obesity has also been linked to poor health-related quality of life.²⁰ Thus, obesity can not only directly increase cancer risk, it can do so indirectly by bringing about emotions or misperceptions that delay or deter preventive screening practices for cancer.

Cancer Incidence and Mortality in Obese Individuals

This epidemic of obesity impacts numerous chronic diseases and medical conditions. Cardiovascular diseases (CVD) and Type-II diabetes mellitus are the diseases most commonly thought to be affected by a patient's obesity.¹⁰ However, recent research has highlighted its impact on cancer as well. In one large study, obesity was recently found to be associated with higher breast cancer mortality rates as well as overall total cancer mortality.²¹ The study followed more than 900,000 healthy U.S. adults (404,576 men and 495,477 women, mean age 57 at enrollment) from 1982 to 1998. Over that 16 year period there were 57,145 deaths from cancer. In persons with a BMI > 40 , death rates from all cancers were 52% higher (for men) and 62% higher (for women) than the death rates for men and women with a normal BMI. Among never smokers with a BMI > 40 , these differentially higher cancer mortality rates were even higher (68% higher in obese men and 88% in obese women). Also, for both genders a higher BMI was significantly associated with certain site-specific cancer death rates, including cancer of the esophagus, colon and rectum, liver, gallbladder, pancreas, kidney, as well as non-Hodgkin's lymphoma and multiple myeloma. Within each gender, a high BMI was related to deaths from cancers of the stomach and prostate for men, and cancer of the breast, uterus, cervix, and ovary for women. The authors conclude that over 90,000 cancer deaths a year could be prevented if adults maintained a normal weight.²¹

The association between obesity and breast cancer differs according to the menopausal status of the women, with postmenopausal women having a higher risk than premenopausal women.²²⁻²⁶ The Women's Health Initiative found postmenopausal women (BMI > 31.1), who were heavier and who had not used hormone replacement therapy, had the highest relative risk of breast cancer (RR = 2.52

(95% CI = 1.62-3.93), after adjusting for age, education, age at menopause, parity, family history of breast cancer, smoking, race, alcohol, diet, and physical activity.²⁴ A longitudinal study of almost half a million women followed for 14 years attributed 30-50% of the breast cancer deaths among postmenopausal women to obesity.²³ A case-control study of over 5,000 women showed that obesity and physical inactivity accounted for 41% of the breast cancer cases in postmenopausal women.²⁷ In contrast, physical activity, irrespective of BMI level, has been shown to lower breast cancer risk.²⁸⁻³⁰ Since many overweight premenopausal women continue to gain weight after menopause, it is important for both premenopausal and postmenopausal women to have a healthy lifestyle that will help them control their weight as they age.

Clinical Recommendations

National surveys report that 12% of adults reported being advised by their doctor, nurse, or other health professional to lose weight.³¹ Some reported being told to maintain or gain weight; but, a high proportion of adults (85%) reported their provider had not given them advice about their weight.³¹ A comparable percentage (84%) of adults living in Hawaii reported their physician had not recently advised them about their weight.³¹ For obese patients, 32% have reported being advised by a health care provider to lose weight, with slightly more (47%) obese patients with comorbidities reporting they were advised to lose weight.³² Similarly, national surveys indicate that physicians rarely counsel adults about physical activity or nutrition.^{33,34}

A first step for clinicians, who want to help patients become aware of their obesity-related risks, is for the physician or his/her staff to measure the patient's height and weight at every visit. Next, the physician should objectively classify the patients' BMI as normal, overweight, or obese (e.g., showing a BMI table to the patient and helping him/her understand how to interpret the BMI categories). To emphasize the importance of weight management to the patient's current and future health and well-being, the clinician should provide clear unequivocal advice about a patient's level of obesity, and the increased risk for chronic diseases, including cancer, that excess weight connotes. Overweight/obesity should be listed on the patient's "problem-list", or the equivalent, so it can be an ongoing issue addressed over time.

The next step should be to ask the patient about the lifestyle factors that are contributing to the patient's excess body weight and provide brief advice, and/or provide referrals, in order to help patients control their weight. For example, advising overweight, sedentary patients to become more active and to eat more fruits, vegetables, and fiber could help them control their weight and potentially lower their cancer risks. Over a quarter of the adults living in Hawaii are sedentary and they eat an average of 3.8 servings of fruits and vegetables a day.¹² Also, national data indicates that 16-24% of overweight adults who are trying to lose weight actually meet the national guidelines for physical activity.³⁵

Why should clinicians spend time talking to their patients about physical activity or exercise? Higher levels of physical activity and fitness are associated with decreased chronic disease incidence and mortality, including colon and breast cancer.^{30,36-43} Blair and colleagues' investigation of all-cause mortality showed that higher fitness levels were associated with lower mortality comparable to

that seen for smoking cessation.⁴⁴ Also, the inverse association between level of fitness and total mortality was found across all levels of body mass index, after controlling for other coronary heart disease risk factors.⁴⁵ Higher levels of physical activity are also related to greater longevity, even after a diagnosis of breast cancer.⁴⁵⁻⁴⁸ A greater level of fitness can promote enhanced functional independence, mental well-being, and improved quality of life for persons throughout the life span.^{49,50} Recent studies indicate that brisk walking and short frequent bouts of activity may be as beneficial as high intensity activities^{51,52} and may facilitate long-term adherence to an exercise regimen.^{45,53,54} Also, studies of physician advice about increasing physical activity have shown that brief advice from a physician coupled with referral to a health educator is particularly effective at increasing the fitness levels of women.^{55,56}

Discussing a patient's dietary intake can be complex and time consuming. However, assessing just a few dietary components, such as daily intake of fruits/vegetables and whole grains, can provide information the clinician can use to help the patient control his or her weight and reduce cancer risk. Several recent epidemiological studies have shown that a diet high in fiber is associated with substantial reductions in coronary heart disease risk, Type II diabetes mellitus risk, and colorectal cancer risk.⁵⁷⁻⁶⁴ A diet high in fiber, across all levels of fat intake, has been associated with less weight gain over a 10 year period in both men and women.⁶⁵ Negative associations have been found between fruit /vegetable intake and CVD as well as cancer.⁶⁶⁻⁶⁸ These and numerous other studies led consensus groups and health organizations in the U.S. and Europe to recommend that adults consume >5 portions of fruits and vegetables a day.^{69,70} Physician advice about both exercise and fruit/vegetable intake was recently shown to improve diet and exercise habits of patients seen in primary care settings.^{71,72}

Combining exercise with reductions in dietary fat and total caloric intake has been shown to be one of the most effective ways to achieve weight loss.⁷³⁻⁷⁷ However, once weight loss has been achieved it can be difficult for patients to maintain their new weight. There are resources on the internet that provide physicians and patients with information on weight management. Two excellent internet resources are: <http://www.surgeongeneral.gov/topics/obesity/default.htm> and http://www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm.

It is beyond the scope of this article to provide in-depth information about the issues surrounding the success rates for various weight-loss programs or special diets. But, making gradual, sustainable changes in diet, especially increasing daily fruits and vegetables, and initiating moderate intensity exercise could help patients avoid future weight gain. Although a patient's weight can be an emotional issue to address with patients, clinicians need to consider that controlling weight gain and encouraging weight loss in overweight/obese individuals can precipitate a "domino" preventive effect across a range of chronic diseases, including cancer, and could potentially increase the patient's longevity. By objectively assessing the patient's weight / BMI level and providing unambiguous advice about the importance of weight control, a clinician can also "set the stage" for future discussions about weight, diet, or exercise.

For more information about the Cancer Research Center of Hawaii, please visit our website at www.crch.org.

References

1. Arias, E., Anderson, R.N., Kung, H.-C., Murphy, S.L., and Kochanek, K.D., Deaths: Final Data for 2001. National Vital Statistics Reports, 2003. 52(3): 1-115.
2. McGinnis, J.M. and Foege, W.H., Actual causes of death in the United States. Journal of the American Medical Association, 1993. 270: 2207-12.
3. Allison, D.B., Fontaine, K.R., Manson, J.E., Stevens, J., and VanItallie, T.B., Annual deaths attributable to obesity in the United States. Journal of the American Medical Association, 1999. 282(16): 1530-8.
4. United States Census Bureau, Census 2000 Data for the State of Hawaii. 2002, Public Information Office, website. <http://www.census.gov/census2000/states/hi.html>, May 7, 2003
5. Hawaii Department of Health, Leading Causes of Death - Hawaii. 1999, Department of Health, website. http://www.state.hi.us/doh/stats/ls_lcd.html.
6. Glanz, K., Croyle, R.T., Chollette, V.Y., and Pinn, V.W., Cancer-related health disparities in women. American Journal of Public Health, 2003. 93(2): 292-8.
7. Hernandez, B.Y., Highlights of recent cancer incidence data in Hawaii. Hawaii Med J, 2003. 62(1): 17-8.
8. Hawaii Tumor Registry, Cancer Incidence for State of Hawaii for years 1975-2000. 2003, Cancer Research Center of Hawaii: Honolulu. 1-55.
9. Vainio, H. and Bianchini, F., eds. Weight Control and Physical Activity. IARC Handbooks of Cancer Prevention. Vol. 6. 2002, International Agency for Research on Cancer, World Health Organization: Lyon.
10. National Institutes of Health, The practical guide. Identification, evaluation, and treatment of overweight and obesity in Adults, ed. F. Xavier Pi-Sunyer. Vol. 00-4084. 2000, Washington DC.: U.S. Department of Health and Human Services.
11. Ahluwalia, I.B., Mack, K.A., Wilmon, W., Mokdad, A.H., and Bales, V.S., State-specific prevalence of selected chronic disease-related characteristics-- Behavioral Risk Factor Surveillance System, 2001. Morbidity and Mortality Weekly Report (Surveillance Summaries), 2003. 52(S08): 1-80.
12. Reyes-Salvail, F., Lu, X., and Chen, J.H., Hawaii Behavioral Risk Factors Surveillance Report. 1994-2000, Hawaii Progress Toward a Healthy People 2000. 2002, Hawaii Department of Health, Community Health Division: Honolulu.
13. Grandinetti, A., Chang, H.K., Chen, R., Fujimoto, W.Y., Rodriguez, B.L., and Curb, J.D., Prevalence of overweight and central adiposity is associated with percentage of indigenous ancestry among native Hawaiians. Int J Obes Relat Metab Disord, 1999. 23(7): 733-7.
14. Maes, H.H., Neale, M.C., and Eaves, L.J., Genetic and environmental factors in relative body weight and human adiposity. Behav Genet, 1997. 27(4): 325-51.
15. Platte, P., Papanicolaou, G.J., Johnston, J., Klein, C.M., Doheny, K.F., Pugh, E.W., Roy-Gagnon, M.H., Stunkard, A.J., Francmano, C.A., and Wilson, A.F., A study of linkage and association of body mass index in the Old Order Amish. Am J Med Genet, 2003. 121C(1): 71-80.
16. Coady, S.A., Jaquish, C.E., Fabsitz, R.R., Larson, M.G., Cupples, L.A., and Myers, R.H., Genetic variability of adult body mass index: a longitudinal assessment in Framingham families. Obes Res, 2002. 10(7): 675-81.
17. Bulik, C.M., Sullivan, P.F., and Kendler, K.S., Genetic and environmental contributions to obesity and binge eating. Int J Eat Disord, 2003. 33(3): 293-8.
18. Wee, C.C., McCarthy, E.P., Davis, R.B., and Phillips, R.S., Screening for cervical and breast cancer: is obesity an unrecognized barrier to preventive care? Ann Intern Med, 2000. 132(9): 697-704.
19. Fontaine, K.R., Heo, M., and Allison, D.B., Body weight and cancer screening among women. J Womens Health Gend Based Med, 2001. 10(5): 463-70.
20. Hassan, M.K., Joshi, A.V., Madhavan, S.S., and Amonkar, M.M., Obesity and health-related quality of life: a cross-sectional analysis of the US population. Int J Obes Relat Metab Disord, 2003. 27(10): 1227-32.
21. Calle, E.E., Rodriguez, C., Walker-Thurmond, K., and Thun, M.J., Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. Adults. New England Journal of Medicine, 2003. 348(17): 1625-38.
22. Berglund, G., Anthropometry, physical activity, and cancer of the breast and colon, in Nutrition and Lifestyle: opportunities for cancer prevention, E. Riboli and R. Lambert, Editors. 2002, International Agency for Research on Cancer, World Health Organization: Lyon, France. p. 237-41.
23. Petrelli, J.M., Calle, E.E., Rodriguez, C., and Thun, M.J., Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of US women. Cancer Causes and Control, 2002. 13(4): 325-32.
24. Morimoto, L.M., White, E., Chen, Z., Chlebowski, R.T., Hays, J., Kuller, L., Lopez, A.M., Manson, J., Margolis, K.L., Muti, P.C., Stefanick, M.L., and McTiernan, A., Obesity, body size, and risk of postmenopausal breast cancer: the Women's Health Initiative (United States). Cancer Causes Control, 2002. 13(8): 741-51.
25. van den Brandt, P.A., Spiegelman, D., Yaun, S.S., Adams, H.O., Beeson, L., Folsom, A.R., Fraser, G., Goldbohm, R.A., Graham, S., Kushi, L., Marshall, J.R., Miller, A.B., Rohan, T., Smith-Warner, S.A., Speizer, F.E., Willett, W.C., Wolk, A., and Hunter, D.J., Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. Am J Epidemiol, 2000. 152(6): 514-27.
26. Lahmann, P.H., Lissner, L., Gullberg, B., Olsson, H., and Berglund, G., A prospective study of adiposity and postmenopausal breast cancer risk: the Malmö Diet and Cancer Study. Int J Cancer, 2003. 103(2): 246-52.
27. Mezzetti, M., La Vecchia, C., Decarli, A., Boyle, P., Talamini, R., and Franceschi, S., Population attributable risk for breast cancer: diet, nutrition, and physical exercise. J Natl Cancer Inst, 1998. 90(5): 389-94.
28. Verloop, J., Rookus, M.A., van der Kooy, K., and van Leeuwen, F.E., Physical activity and breast cancer risk in women aged 20-54 years. J Natl Cancer Inst, 2000. 92(2): 128-35.
29. Friedenreich, C.M., Courneya, K.S., and Bryant, H.E., Case-control study of anthropometric measures and breast cancer risk. Int J Cancer, 2002. 99(3): 445-52.
30. Thune, I. and Furberg, A.S., Physical activity and cancer risk: dose-response and cancer, all sites and site-specific. Med Sci Sports Exerc, 2001. 33(6 Suppl): S530-50; discussion S609-10.
31. Behavioral Risk Factors Surveillance System (BRFSS), BRFSS Prevalence Data, weight control -2000., 2003, Centers for Disease Control and Prevention, website. <http://www.cdc.gov/brfss/>, August 28, 2003
32. Sciamanna, C.N., Tate, D.F., Lang, W., and Wing, R.R., Who reports receiving advice to lose weight? Results from a multistate survey. Arch Intern Med, 2000. 160(15): 2334-9.
33. Wee, C.C., McCarthy, E.P., Davis, R.B., and Phillips, R.S., Physician counseling about exercise. Journal of the American Medical Association, 1999. 282(16): 1583-8.
34. Centers for Disease Control and Prevention, Missed opportunities in preventive counseling for cardiovascular disease - United States. Morbidity and Mortality Weekly Report, 1998. 47: 91-5.

35. Centers for Disease Control and Prevention. Prevalence of leisure-time physical activity among overweight. United States, 1998. Morbidity and Mortality Weekly Report. 2000. 49(15): 326-30.
36. Blair, S.N., Kohl, H.W., III, Barlow, C.E., Paffenbarger, R.S.J., Gibbons, L.W., and Macera, C.A., Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. *Journal of the American Medical Association*, 1995. 273: 1093-8.
37. Wannamethee, S.G. and Shaper, A.G., Physical activity in the prevention of cardiovascular disease: an epidemiological perspective. *Sports Medicine*, 2001. 31(2): 101-14.
38. Lee, I. and Skerrett, P.J., Physical activity and all-cause mortality: what is the dose-response relation? *Medicine and Science in Sports and Exercise*, 2001. 33(6, suppl.): S459-S71.
39. Rockhill, B., Willett, W.C., Manson, J.E., Leitzmann, M.F., Stampfer, M.J., Hunter, D.J., and Colditz, G., Physical activity and mortality: a prospective study among women. *American Journal of Public Health*, 2001. 91(4): 578-83.
40. Lee, I.-M. and Paffenbarger, R.S., Associations of light, moderate, and vigorous intensity physical activity with longevity: the Harvard Alumni Health Study. *American Journal of Epidemiology*, 2000. 151(3): 293-9.
41. Villeneuve, P.J., Morrison, H.I., Craig, C.L., and Schaubel, D.E., Physical activity, physical fitness, and risk of dying. *Epidemiology*, 1998. 9: 626-31.
42. Dirx, M.J., Voorrips, L.E., Goldbohm, R.A., and van den Brandt, P.A., Baseline recreational physical activity, history of sports participation, and postmenopausal breast carcinoma risk in the Netherlands Cohort Study. *Cancer*, 2001. 92(6): 1638-49.
43. Slattery, M.L. and Potter, J.D., Physical activity and colon cancer: confounding or interaction? *Med Sci Sports Exerc*, 2002. 34(6): 913-9.
44. Blair, S.N., Kampert, J.B., Kohl, H.W., Barlow, C.E., Macera, C.A., Paffenbarger, R.S., and Gibbons, L.W., Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women. *Journal of the American Medical Association*, 1996. 276: 205-10.
45. Blair, S.N., Kohl, H.W.I., Paffenbarger, R.S.J., Clark, D.G., Cooper, K.H., and Gibbons, L.W., Physical fitness and all-cause mortality: a prospective study of healthy men and women. *Journal of the American Medical Association*, 1989. 262: 2395-401.
46. Blair, S., Cheng, Y., and Holder, S., Is physical activity or physical fitness more important in defining health benefits? *Medicine and Science in Sports and Exercise*, 2001. 33(6, suppl.): S379-S99.
47. Lissner, L., Bengtsson, C., Bjorkelund, C., and Wedel, H., Physical activity levels and change in relation to longevity: A prospective study of Swedish women. *American Journal of Epidemiology*, 1996. 143: 54-62.
48. Zhang, S., Folsom, A.R., Sellers, T.A., Kushi, L.H., and Potter, J.D., Better breast cancer survival for postmenopausal women who are less overweight and eat less fat. The Iowa Women's Health Study. *Cancer*, 1995. 76(2): 275-83.
49. DiLorenzo, T.M., Bargman, E.P., Stucky-Ropp, R., Brassington, G.S., Frensch, P.A., and LaFontaine, T., Long-term effects of aerobic exercise on psychological outcomes. *Preventive Medicine*, 1999. 28(75-85).
50. United States Department of Health and Human Services, Physical activity and health: a report of the Surgeon General. 1996. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion: Atlanta, GA.
51. Manson, J.E., Hu, F.B., Rich-Edwards, J.W., Colditz, G.A., Stampfer, M.J., Willett, W.C., Speizer, F.E., and Hennekens, C.H., A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *New England Journal of Medicine*, 1999. 341: 650-8.
52. Mensink, G.B.M., Heerstrass, D.W., Neppelenbroek, S.D., Schuit, A.J., and Bellach, B.-M., Intensity, duration, and frequency of physical activity and coronary risk factors. *Medicine and Science in Sports and Exercise*, 1997. 29(9): 1192-8.
53. Jakicic, J.M., Wing, R.R., Butler, B.A., and Robertson, R.J., Prescribing exercise in multiple short bouts versus one continuous bout: effects on adherence, cardiorespiratory fitness, and weight loss in overweight women. *International Journal of Obesity*, 1995. 19: 893-901.
54. Coleman, K.J., Raynor, H.R., Mueller, D.M., Cerny, F.J., Dorn, J.M., and Epstein, L.H., Providing sedentary adults with choices for meeting their walking goals. *Preventive Medicine*, 1999. 28: 510-9.
55. Albright, C.L., Cohen, S., Gibbons, L., Miller, S., Marcus, B., Sallis, J., Imai, K., Jernick, J., and Simons-Morton, D.G., Incorporating physical activity advice into primary care: physician-delivered advice within the activity counseling trial. *Am J Prev Med*, 2000. 18(3): 225-34.
56. Simons-Morton, D.G., Morgan, T., Haskell, W., King, A., Applegate, W., Blair, S., Albright, C.L., Cohen, S., Ribisl, P., O'Toole, M., and Shih, J., Results of the Activity Counseling Trial: A randomized controlled trial of physical activity counseling in primary care. *Journal of the American Medical Association*, 2001. 286: 677-87.
57. Wolk, A., Manson, J.E., Stampfer, M., Colditz, G.A., Hu, F.B., Speizer, F.E., Hennekens, C.H., and Willett, W.C., Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *Journal of the American Medical Association*, 1999. 281(21): 1998-2004.
58. Salmeron, J., Manson, J.E., Stampfer, M.J., Colditz, G.A., Wing, A.L., and Willett, W.C., Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women [see comments]. *Journal of the American Medical Association*, 1997. 277(6): 472-7.
59. Jacobs, D.R., Meyer, K.A., Kushi, L.H., and Folsom, A.R., Is the whole grain intake associated with reduced total and cause-specific death rates in older women? The Iowa Women's Health Study. *American Journal of Public Health*, 1999. 89(3): 322-9.
60. Liu, S., Manson, J.E., Stampfer, M., Hu, F.B., Giovannucci, E., Colditz, G.A., Hennekens, C.H., and Willett, W.C., A prospective study of whole-grain intake and risk of Type 2 Diabetes in U.S. women. *American Journal of Public Health*, 2000. 90(9): 1409-15.
61. Salmeron, J., Ascherio, A., Rimm, E.B., Colditz, G.A., Spiegelman, D., Jenkins, D.J., Stampfer, M.J., Wing, A.L., and Willett, W.C., Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care*, 1997. 20(4): 545-50.
62. Peters, U., Sinha, R., Chatterjee, N., Subar, A.F., Ziegler, R.G., Kulldorff, M., Bresalier, R., Weissfeld, J.L., Flood, A., Schatzkin, A., and Hayes, R.B., Dietary fibre and colorectal adenoma in a colorectal cancer early detection programme. *Lancet*, 2003. 361(9368): 1491-5.
63. Bingham, S.A., Day, N.E., Luben, R., Ferrari, P., Slimani, N., Norat, T., Clavel-Chapelon, F., Kesse, E., Nieters, A., Boeing, H., Tjonneland, A., Overvad, K., Martinez, C., Dorronsoro, M., Gonzalez, C.A., Key, T.J., Trichopoulou, A., Naska, A., Vineis, P., Tumino, R., Krogh, V., Bueno-de-Mesquita, H.B., Peeters, P.H., Berglund, G., Hallmans, G., Lund, E., Skeie, G., Kaaks, R., and Riboli, E., Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet*, 2003. 361(9368): 1496-501.
64. Ford, E.S. and Mokdad, A.H., Fruit and vegetable consumption and diabetes mellitus incidence among U.S. adults. *Prev Med*, 2001. 32(1): 33-9.
65. Ludwig, D.S., Periera, M.A., Kroenke, C.H., Hilner, J.E., Van Horn, L., Slattery, M.L., and Jacobs, D.R., Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *Journal of the American Medical Association*, 1999. 282(16): 1539-46.
66. Joshipura, K.J., Ascherio, A., Manson, J.E., Stampfer, M., Rimm, E.B., Speizer, F.E., Hennekens, C.H., Spiegelman, D., and Willett, W.C., Fruit and vegetable intake in relation to risk of Ischemic stroke. *Journal of the American Medical Association*, 1999. 282(13): 1233-9.
67. Ness, A.R. and Powles, J.W., Fruit and vegetables, and cardiovascular disease: a review. *International Journal of Epidemiology*, 1997. 26(1): 1-13.
68. Steinmetz, K.A. and Potter, J.D., Vegetables, fruit, and cancer. I. *Epidemiology. Cancer Causes and Control*, 1991. 2: 325-57.
69. National Research Council, Diet and Health. 1989. Washington, D.C.: National Academy Press.
70. United States Department of Agriculture, Nutrition and your health. Dietary guidelines for Americans. 2000. Washington, DC: U.S. Department of Health and Human Services.
71. Calfas, K.J., Sallis, J.F., Zabinski, M.F., Wilfley, D.E., Rupp, J., Prochaska, J.J., Thompson, S., Pratt, M., and Patrick, K., Preliminary evaluation of a multicomponent program for nutrition and physical activity change in primary care: PACE+ for adults. *Prev Med*, 2002. 34(2): 153-61.
72. Ockene, J.S., Hebert, J.R., Ockene, J.K., Saperia, G.M., Stanek, E., Nicolosi, R., Merriam, P.A., and Hurley, T.G., Effect of physician-delivered nutrition counseling training and an office-support program on saturated fat intake, weight, and serum lipid measurements in a hyperlipidemic population: Worcester Area Trial for Counseling in Hyperlipidemia (WATCH). *Arch Intern Med*, 1999. 159(7): 725-31.
73. Miller, W.C., How effective are traditional dietary and exercise interventions for weight loss? *Med. Sci in Sports Exerc*, 1999. Aug;31(8): 1129-34.
74. Jeffery, R.W., Drenowski, A., Epstein, L.H., Stunkard, A.J., Wilson, G.T., Wing, R.R., and Hill, D.R., Long-term maintenance of weight loss: current status. *Health Psychol*, 2000. 19(1 Suppl): 5-16.
75. Wing, R.R., Physical activity in the treatment of the adulthood overweight and obesity: current evidence and research issues. *Medicine and Science in Sports and Exercise*, 1999. 31(11-suppl): S547-52.
76. Jakicic, J.M., Marcus, B.H., Gallagher, K.I., Napolitano, M., and Lang, W., Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *Journal of the American Medical Association*, 2003. 290(10): 1323-30.
77. Donnelly, J.E., Hill, J.O., Jacobsen, D.J., Potteiger, J., Sullivan, D.K., Johnson, S.L., Heelan, K., Hise, M., Fennessey, P.V., Sonko, B., Sharp, T., Jakicic, J.M., Blair, S.N., Tran, Z.V., Mayo, M., Gibson, C., and Washburn, R.A., Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med*, 2003. 163(11): 1343-50.



Aloha Laboratories, Inc.
...When results count

**A CAP accredited laboratory
 specializing in Anatomic
 Pathology
 Quality and Service**

**David M. Amberger, M.D.
 Laboratory Director**

Phone: (808) 842-6600

Fax: (808) 848-0663

E-Mail: results@alohalabs.com

<http://www.alohalabs.com>